

In the Specification:

Please amend the specification as follows:

On page 4, please replace the third full paragraph with the following replacement paragraph:

(b)

While the new MALDI techniques opened the field of biomolecular mass spectrometry, the mass spectrometric analysis of complex biological materials was not possible because of matrix overloading. Recently, Hutchens et al. (Hutchens, T.W. and Yip, T., Rapid Communications in Mass Spectrometry, vol 7, 1993, pp. 576-580.) demonstrated the utilization of affinity capture methods to quasi-purify proteins in a specimen prior to MALDI mass spectrometry. By quasi-purifying the specimen being assayed Hutchens et al. effectively overcame the primary limitation of MALDI mass spectrometry, namely, the suppression of ion signal due to overloading of the matrix. They named their technique "surface-enhanced affinity capture mass spectrometry (SEAC)". They further demonstrated their technique by using single stranded DNA which they immobilized on the mass spectrometer probe tip to quasi-isolate the protein lactoferrin from preterm infant urine.

At page 5, please replace the fourth paragraph with the following replacement paragraph:

(b) 2

The present invention combines and exploits the specificity of antibody-antigen binding and the ability of the mass spectrometer to unequivocally identify molecules in various qualitative and quantitative strategies to analyze one or more antigens or antibodies in a specimen within the limit of detection. Both qualitative and quantification quantitative strategies utilize an antibody or antigen to capture and isolate another antigen or antibody, respectively, from its surroundings, and thereafter mass spectrometrically analyze the isolated antibody or antigen after release from the capturing agent. This specificity of the antibody-antigen reaction coupled with the ability of the mass spectrometer to separate and unequivocally identify the captured and isolated antibody or antigen by its mass-to-charge ratio from other molecules that may accompany it lends two dimensions of specificity to the present invention.

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At page 6, please replace the third paragraph with the following replacement paragraph:

An article by Nelson, R., et al., published in Analytical Chemistry, vol. 67, pp 1153-1158, on or about March 31, 1995, describes certain portions of the present invention in detail and is herein incorporated by reference.

At page 17, please replace the first full paragraph with the following replacement paragraph:

b4

"Solid substrate" is defined as any physically separable solid to which an antibody or antigen can be directly or indirectly attached including but not limited to agarose beads, nylon, metals, glass, silicon, and organic membranes.

At page 36, please replace the first full paragraph with the following replacement paragraph:

b5

The analyte/IRS signal ratios in the addition-present mass spectral signals are then used to determine the analyte concentration in the addition-absent sample exactly as in the parallel standard addition approach. Since mass spectrometric immunoassay of each addition-present sample serves to calibrate a sample in which the concentration of the analyte differs from the analyte concentration in the addition-free sample by an amount which depends on the amounts of analyte captured in the preceding mass spectrometric immunoassays, it is apparent that the accuracy of this procedure will only be acceptable if the amount of analyte captured in each successive step is small, for example if 5% of the analyte is captured in the mass spectrometric immunoassay of the addition-free sample and mass spectrometric immunoassay of a single addition-present sample is performed, the analyte concentration determined thereby would be in error by 5%.

At page 41, please replace the second full paragraph with the following replacement paragraph:

ble

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry of the dried material on the mass spectrometer probe tip was then performed on a linear time-of-flight mass spectrometer. The instrument consisted of a 30 kilovolt two-stage acceleration source followed by a 1.4-meter field free drift region containing a particle wire guide. A frequency-tripled Nd:YAG (355

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nm) LUMONICS HY 400 laser (Lumonics HY 400) was used for desorption/ionization. Ion signals were detected using a hybrid microchannel plate/discrete dynode electron multiplier and recorded using a 500 MS/s transient recorder (TEKTRONIX TDS 520A) capable of fast signal averaging. The laser irradiance was adjusted during signal averaging while monitoring the mass spectra on a sampling oscilloscope (TEKTRONIX TDS 310), in order to achieve optimum ion signal (significant signal versus maximum resolution). Time-of-flight spectrum was generated by signal averaging 50 laser shots into a single spectrum and transferring the data to an IBM compatible personal computer. Data was processed using the commercially available software, LABCALC (Galactic Industries). The time-of-flight mass spectrum was obtained in the positive ion mode and externally calibrated with a calibration equation generated using horse heart cytochrome c (molecular weight (MW) of 12,360 Da).

At page 46, please replace the third full paragraph with the following replacement paragraph:

b7

An analytical sample, known to contain 12.5 nM AlAG was mass spectrometrically immunoassayed under similar conditions for the preparations above. The resulting AlAG signal was within that represented on the 5-point working curve of **FIG. 9** and is shown at point -O- corresponding to an AlAG concentration of ~12.5 nM which verifies the accuracy of the working curve quantification method.